PATENT COOPERATION TREATY

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:

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PCT

WRITTEN OPINION
(PCT Rule 66)

Date of mailing *(day/month/year)*	18.05.2004
Applicant's or agent's file reference 03/084 PCT	**REPLY DUE** within 1 month(s) from the above date of mailing

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/EP 03/03353	28.03.2003	28.03.2002

International Patent Classification (IPC) or both national classification and IPC
A61K39/00

Applicant
BRENNTAG BIOSECTOR A/S

1. This written opinion is the **first** drawn up by this International Preliminary Examining Authority.

2. This opinion contains indications relating to the following items:

I	☒	Basis of the opinion
II	☐	Priority
III	☐	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
IV	☐	Lack of unity of invention
V	☒	Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
VI	☐	Certain documents cited
VII	☐	Certain defects in the international application
VIII	☐	Certain observations on the international application

3. The applicant is hereby **invited to reply** to this opinion.

When? See the time limit indicated above. The applicant may, before the expiration of that time limit, request this Authority to grant an extension, see Rule 66.2(d).

How? By submitting a written reply, accompanied, where appropriate, by amendments, according to Rule 66.3. For the form and the language of the amendments, see Rules 66.8 and 66.9.

Also: For an additional opportunity to submit amendments, see Rule 66.4.
For the examiner's obligation to consider amendments and/or arguments, see Rule 66.4 bis.
For an informal communication with the examiner, see Rule 66.6.

If no reply is filed, the international preliminary examination report will be established on the basis of this opinion.

4. The final date by which the international preliminary examination report must be established according to Rule 69.2 is: 28.07.2004

Name and mailing address of the international preliminary examining authority:

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I. **Basis of the opinion**

With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this opinion as "originally filed")*:

Description, Pages

1-13 as originally filed

Claims, Numbers

1-9 as originally filed

Drawings, Sheets

1/1 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

   These elements were available or furnished to this Authority in the following language: , which is:

   ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
   ☐ the language of publication of the international application (under Rule 48.3(b)).
   ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

   ☐ contained in the international application in written form.
   ☐ filed together with the international application in computer readable form.
   ☐ furnished subsequently to this Authority in written form.
   ☐ furnished subsequently to this Authority in computer readable form.
   ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
   ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

   ☐ the description, pages:
   ☐ the claims, Nos.:
   ☐ the drawings, sheets:

5. ☐ This opinion has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

6. Additional observations, if necessary:

V. Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	1-3,5,9
Inventive step (IS)	Claims	1-6,8,9
Industrial applicability (IA)	Claims	

2. Citations and explanations

see separate sheet

Re Item V

Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

CITED DOCUMENTS

The following documents are referred to in this communication; the numbering will be adhered to in the rest of the procedure:

D1: WO 99 30733 A (SMITHKLINE BEECHAM BIOLOGICALS S.A.) 24 June 1999 (1999-06-24)
D2: WO 00 02591 A (MERCK & CO, INC.) 20 January 2000 (2000-01-20)
D3: WO 97 28818 A (THEREXSYS LIMITED) 14 Augustus 1997 (1997-08-14)
D4: WO 00 68259 A (G. LINDAHL) 16 November 2000 (2000-11-16)
D5: WO 93 24148 A (SMITHKLINE BEECHAM BIOLOGICALS (S.A.)) 9 December 1993 (1993-12-09)

1. NOVELTY (Article 33(2) PCT)

1.1. *D1* discloses simultaneous vaccination with DNA and protein. May be adjuvanted with aluminium phosphate (see page 9, lines 18-27, and the claims).

D2 discloses a vaccine composition comprising (a) a polynucleotide vaccine component, e.g. encoding HBsAg or influenza virus, and (b) a mineral-based adjuvant, e.g. aluminium or calcium phosphate. Said vaccine composition may additionally include antigenic protein (see page 20, lines 21-27).

D3 discloses a combination (mixture or complex) for vaccination, comprising a nucleic acid encoding a first epitope and a peptide containing a second epitope. May be combined with an adjuvant, e.g. aluminium phosphate.

1.2. Hence, the subject-matter of present claims **1-3, 5** and **9** is not new in the sense of Article 33(2) PCT.

1.3. In view of the prior art cited, present claims **4** and **6-8** appear to be novel and meet

therefore the requirements of Article 33(2) PCT.

2. INVENTIVE STEP (Article 33(3) PCT)

With regard to present claim **7**, *D1* is considered to represent the most relevant state of the art and discloses the simultaneous vaccination with DNA and protein. This mixture or complex may be adjuvanted with aluminium phosphate (see page 9, lines 18-27, and the claims).

The subject-matter of present claim **7** differs in that the mineral-based negatively charged adjuvant is preincubated or subsequently mixed with said at least protein antigen vaccine prior to being formulated with said polynucleotide vaccine component.

The problem to be solved by the present invention may therefore be regarded as providing a vaccine composition in which the mineral-based negatively-charged adjuvant-mediated enhancement of the immunogenicity of DNA vaccines is further improved.

The proposed solution is a vaccine composition wherein the mineral-based negatively-charged adjuvant is preincubated or subsequently mixed with at least one protein antigen vaccine component prior to being formulated with the polynucleotide vaccine component.

2.3. This solution has not been disclosed, nor suggested, in the prior art, and, hence, the subject-matter of present claim **7** involves an inventive step in the sense of Article 33(3) PCT.

Present claim **8** differs from the disclosure of *D1* in that it refers to a kit. For a person skilled in the art, grouping the materials used for a series of known or obvious experiments in the form of a kit is, however, not inventive.

Present dependent claim **4** does not appear to contain any additional features which, in combination with the features of any claim to which they refer, involve an inventive step for the following reasons:

D4 discloses a.o. the use of bovine serum albumin as a model protein antigen in a vaccination procedure (see page 27, lines 5-8, page 29, lines 7-9).

Therefore, serum albumin for use as a model protein antigen in a vaccine composition is merely one of several straightforward possibilities from which the skilled person would select, in accordance with the circumstances, without the exercise of inventive kill, in order to solve the problem posed.

2.6. Present dependent claim **6** does not appear to contain any additional features which, in combination with the features of any claim to which they refer, involve an inventive step for the following reasons:

D5 discloses a combined vaccine composition comprising HBsAg and a variety of other antigens, one of which is inactivated polio virus (see page 3, lines 8-12)

Therefore, inactivated polio virus, for use in a vaccine composition, is merely one of several straightforward possibilities from which the skilled person would select, in accordance with the circumstances, without the exercise of inventive kill, in order to solve the problem posed.

2.7. In view of the above, the subject matter of present claims **4, 6** and **8** does not involve an inventive step in the sense of Article 33(3) PCT.

3. FURTHER REMARKS

3.1. In the present claim **7** a method feature is used to characterise a product. This renders the subject matter of this claim unclear in the sense of Article 6 PCT.